AMENDMENTS TO THE DRAWINGS

Figure 11 has been amended to correct an error in the numbering of certain sequence identifiers therein to correspond to the numbering used in the sequence listing and throughout the specification and claims as originally filed. Namely, originally labeled "SEQ ID NO: 24" is now correctly identified as "SEQ ID NO: 22" and originally labeled "SEQ ID NO: 22" is now correctly identified as "SEQ ID NO: 24." In addition, Figure 11 has been amended to correct the identification of the sequences as Amino Acid or Nucleotide sequences. The sequence now labeled as SEQ ID NO: 22 is correctly identified as an "Amino Acid Sequence of Light Chain Variable Region" and the sequence now labeled SEQ ID NO: 24 is now correctly identified as a "Nucleotide sequence of light chain variable region." Please replace original Figure 11, with the Replacement Sheet of Figure 11 enclosed herewith.

REMARKS

Claims 1-19 are pending in the instant application. Claims 1, 3, 6, 10, 14, 15, and 19 have been amended as discussed below. Claim 7 has been amended to correct a typographical error and Claim 8 has been amended to add proper punctuation. New Claims 20-27 have been added. The new claims relate to methods wherein the antibodies have specific combinations of the heavy and light chain polypeptides recited in independent Claims 1, 10, and 15. Claims 1-27 are now pending in the instant application. No new matter has been added by way of these amendments

Sequence Listing

Applicants provide a substitute Sequence Listing attached herewith. The substitute sequence listing adds SEQ ID NOs.: 41-80, which were previously identified in the "Brief Description of the Drawings" and which correspond to the sequences disclosed in Figures 16-35, as well as SEQ ID NOs.: 81-90, which correspond to the sequences disclosed in Figures 28, 29, 36 and Example 1, for which sequence identifiers were added to the specification by way of this amendment.

Please replace the sequence listing as originally filed with the Substitute Sequence listing attached herewith. Applicants state that the contents of the enclosed paper copy of the Sequence Listing are identical to the computer readable form attached herewith.

Specification

Applicants have amended the specification to correct a spelling error on page 4, specifically, the correction of "embodimet" to "embodiment." No new matter has been added by way of this amendment.

Applicants have also amended paragraphs in the Brief Description of the Drawings section of the specification beginning at page 10, line 3, page 10, line 7, and page 11, line 11 to add sequence identifiers. More specifically, the labels "SEQ ID NO: 81," "SEQ ID NO: 82," and "SEQ ID NO:85" through "SEQ ID NO: 90" have been added to identify the sequences in the drawings. Additionally, Applicants have amended the paragraph beginning on page 32, line 25 to correct the numbering of the sequence identifiers to correspond to the numbering used in the

sequence listing. Namely, "SEQ ID NO: 10" and "SEQ ID NO: 11" have been corrected to "SEQ ID NO: 83" and "SEQ ID NO: 84," respectively. No new matter has been added by way of these amendments, as Applicants have merely changed the sequence identifiers that are associated with sequences of record.

The Examiner objected to the specification at page 5, line 3 because a comma is missing after the "5" and a space is missing before the "5." Accordingly, the paragraph beginning on page 4, line 30 has been amended to insert the appropriate comma and space and to correct a spelling error. Applicants have also amended the paragraph beginning on page 4, line 16 and the paragraph beginning on page 4, line 23 to insert a comma after the "5" and a space before the "5." Applicants respectfully request that this objection be withdrawn.

Figure 11

Applicants have amended Figure 11 to correct an error in the numbering of certain sequence identifiers therein to correspond to the numbering used in the sequence listing and throughout the specification, including that used in the description of Figure 11 found on page 7, lines 13-16, and in the claims as originally filed. Additionally, Figure 11 has been amended to correct the identification of the sequences as Amino Acid or Nucleotide sequences. No new matter has been added by way of this amendment.

Claim Objections

The Examiner objected to Claims 1 and 10 because a comma is missing after the "5" and a space is missing before the "5."

Claims 1 and 10 have been amended to insert the appropriate comma and space. Accordingly, Applicants respectfully request that this objection be withdrawn.

Indefiniteness Rejection Under 35 U.S.C. § 112, Second Paragraph

a). The Examiner rejected Claims 1-19 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, the claims are allegedly indefinite

for reciting "comprising a heavy chain amino acid" because it is not clear whether the monoclonal antibody comprises a heavy chain amino acid sequence or just an amino acid, and because the claims do not state that the recited sequences are actually heavy chain sequences.

Applicants have amended independent Claims 1, 10 and 15 to specify that the antibody comprises a heavy chain amino acid sequence. Additionally, Applicants have amended Claims 1, 10 and 15 to specify that he recited sequences are heavy chain sequences. Accordingly, Applicants respectfully request withdrawal of this rejection.

b.) The Examiner rejected Claim 3 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for reciting "light chain amino acid having an amino acid sequence."

Applicants have amended Claim 3 to specify that the antibody comprises a light chain amino acid sequence. Accordingly, Applicants respectfully request withdrawal of this rejection.

c.) The Examiner rejected Claim 3 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for reciting "further comprises a light chain." The Examiner states that because monoclonal antibodies comprise both heavy and light chains, it is unclear what the phrase encompasses. The Examiner notes that amending the claim to delete the term "further" would obviate the rejection.

Applicants have amended Claim 3 as suggested by the Examiner to delete the term "further," thereby obviating this rejection. Accordingly, Applicants respectfully request withdrawal of this rejection.

d.) The Examiner rejected Claim 1 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for reciting the limitation "said cells" because there is insufficient antecedent basis for this limitation in the claim.

Applicants have amended the rejected limitation of Claim 1 to recite, in relevant part, "wherein said contacting results in inhibited growth of said tumor." (Emphasis added.) This

amended limitation has sufficient antecedent basis. Accordingly, Applicants respectfully request withdrawal of this rejection.

e.) The Examiner rejected Claims 6, 14 and 19 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for reciting "the further therapeutic agent" because there is insufficient antecedent basis for this limitation. The Examiner notes that deleting the term "further" would obviate this rejection.

Applicants have amended Claims 6, 14 and 19 as suggested by the Examiner to delete the term "further," thereby obviating this rejection. Accordingly, Applicants respectfully request withdrawal of this rejection.

Enablement Rejection Under 35 U.S.C. § 112, First Paragraph

The Examiner rejected Claims 1-6, 8, 9 and 15-19 under 35 U.S.C. § 112, first paragraph, alleging that the specification, while being enabling for a method of inhibiting melanoma growth/metastasis and lung metastasis in an animal, and a method of inhibiting cell invasion associated with melanoma, and a method of increasing the survival of an animal having melanoma metastasis or lung metastasis does not reasonably provide enablement for a method of inhibiting just any tumor growth/tumor metastasis or just any lung tumor and a method of increasing survival of an animal having just any metastatic tumor. The Examiner asserts that no direction or guidance is provided to assist one skilled in the art to use a monoclonal antibody that binds MUC18 in a method of inhibiting just any tumor growth/metastasis in an animal and a method of increasing the survival of an animal having just any metastatic tumor, which do not necessarily express MUC18. Applicants disagree.

To be enabling, "the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *In re Wright*, 999 F.2d 1557 (Fed. Cir. 1993). Nevertheless, not everything necessary to practice the invention need be disclosed. In fact, what is well-known is best omitted. M.P.E.P. § 2164.08 (citing *In re Buchner*, 929 F.2d 1557 (Fed. Cir. 1993)). Enablement "is not precluded even if some experimentation is necessary, although the amount of experimentation needed must not be

unduly extensive." *See Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367 (Fed. Cir. 1986).

Applicants have amended independent Claims 1 and 15 to specify that the tumors affected by the claimed methods are those that comprise cells expressing MUC18. In view of Applicants' finding of the therapeutic value of inhibiting MUC-18 to treat melanoma cell proliferation and lung metastasis, a person of ordinary skill in the art would recognize that inhibiting the MUC-18 antigen when expressed on other tumor cells would likewise be an effective method for inhibiting growth of such tumors and for increasing survival of animals having these tumors. Applicants respectfully submit that the specification teaches one of skill in the art how to perform the full scope of the claimed method of inhibiting the proliferation of tumor cells expressing MUC18 in an animal and method of increasing survival of an animal having a metastatic tumor that expresses MUC18.

Guidance to enable one of skill in the art to use the invention as claimed can be found throughout the specification and claims as originally filed, for example, on pages 25 through 27 and throughout the Examples section which describe experiments wherein animals having tumors that express MUC18 were contacted with anti-MUC18 antibodies and tumor formation was inhibited and/or survival was increased. Thus, Applicants submit that the specification enables any person skilled in the art to make and/or use the invention commensurate in scope with the amended claims without undue experimentation. Accordingly, Applicants respectfully request that this rejection be withdrawn.

Provisional Obviousness-type Double Patenting Rejection

The Examiner provisionally rejected Claims 1-19 under the judicially created doctrine of obviousness-type double patenting as being allegedly unpatentable over Claims 1-17 of co-pending Application No. 10/330,530.

The judicially created doctrine of obviousness-type double patenting requires that the claims of the rejected application are obvious in view of the claims of the cited co-pending application. Thus, a double patenting rejection of the obviousness-type is "analogous to [a failure to meet] the nonobviousness requirement of 35 U.S.C. § 103 " except that the patent principally underlying the double patenting rejection is not considered prior art. *In re*

Braithwaite, 379 F.2d 594, 154 USPQ 29 (CCPA 1967). Therefore, any analysis employed in an obviousness-type double patenting rejection parallels the guidelines for analysis of a 35 U.S.C. § 103 obviousness determination. *In re Braat*, 937 F.2d 589, 19 USPQ2d 1289 (Fed. Cir. 1991); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Applicants respectfully disagree with this rejection and submit that the claims of the instant application are not obvious in view of Claims 1-17 of co-pending Application No. 10/330,530. The claims of the instant application are drawn to methods of inhibiting tumor growth, inhibiting cell invasion or increasing survival *of an animal*. These methods comprise the step of "selecting an animal", which is not found in the claims of the co-pending application. In contrast, Claims 1-17 of co-pending Application No. 10/330,530 are drawn to methods of inhibiting cell proliferation associated with the expression of the MUC18 tumor antigen by contacting cells expressing MUC18 with a monoclonal antibody that binds MUC18 and incubating these cells in the presence of the antibody. These methods include the step of "incubating said cells and said antibody" which is not found in the instant application. Accordingly, the claims of the co-pending application do not teach or suggest all of the claim limitations of the instant application, and therefore, the claims of the instant application are not obvious in view of the claims of the co-pending application.

Because the claims of the instant application are not obvious in view of Claims 1-17 of co-pending Application No. 10/330,530, Applicants respectfully request that this provisional rejection be withdrawn.

CONCLUSION

The undersigned has made a good faith effort to respond to the Office Action and submits that the application is now in condition for allowance. Nevertheless, if any undeveloped issues remain or if any issues require clarification, the Examiner is invited to call the undersigned attorney to resolve such issues promptly.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: Feb. 16, 2005

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